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June 4, 2003 (Date of Transmission)

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Customer No.: 07278
PATENT TRADEMARK OFFICE

Docket No: 4040/1K200US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Mark I. GREENE *et al.*

Serial No.: 09/627,775 Art Unit: 1655

Confirmation No.: 3099

Filed: July 28, 2000 Examiner: Arun K. CHAKRABARTI

For: METHODS OF INHIBITING OSTEOCLASTOGENESIS

SUPPLEMENTAL COMMUNICATION

Hon. Commissioner of Patents and Trademarks
Washington, DC 20231

S I R:

Pursuant to the request of Examiner Arun K. Chakrabarti, please enter and consider the following remarks. It is believed that no fee is required for this submission. Applicants note that this submission is **NOT** offered as a response to the Office Action mailed on December 27, 2002 for this matter. Instead, this submission is made to provide information specifically requested by the Examiner. Accordingly, it is believed that no Extensions of Time are required and that no fees are owed for this submission.

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However, should the U.S. Patent and Trademark Office determine that any Extensions of Time are required, the Commissioner is hereby authorized and requested to also consider this document as a Petition for the required Extension(s) of Time and that any such required Extension(s) of Time be granted. Should any fee be required for this submission, please charge the required fee(s) to our Deposit Account No. 04-0100.

REMARKS

At the outset, Applicants thank Examiner Arun K. Chakrabarti for the courtesies extended when the Examiner contacted Applicants' undersigned representative by telephone on June 3, 2003. During that telephone conversation, Examiner Chakrabarti requested that applicants specify support in the specification for the pending claim limitation of TNF-R(I), and transmit that information to him in a telefacsimile communication. The Examiner indicated that the pending claims of this application are allowable, provided Applicants can demonstrate adequate support for the TNF-R(I) limitation.

Pursuant to the Examiner's request, Applicants respectfully direct the Examiner's attention, first, to the Examples at the end of this application and, particularly, to Example 2 at pages 36 to 39. These Examples describe, in detail, experiments in which compounds were generated using binding sequences from crystal structures of TNF-R(I), and demonstrate that the compounds inhibit osteoclastogenesis by inhibiting another, different TNF-R superfamily member – RANK. See, in particular, lines 9-27 on page 36 and lines 14-17 on page 37 of this application as filed.

Further support is provided elsewhere in the specification. For example, see the specification at page 4, lines 2-3 and at page 9, lines 23-25. The TNF-R superfamily members are also discussed generally in the specification, *e.g.*, at page 9, lines 13-21. Moreover, exemplary sequences of these TNF-R superfamily members are provided in Figure 1 of the application – including the amino acid sequence for TNF-R(I).

Applicants also wish to respectfully point out that one possible source of confusion for the Examiner may be that these latter sections of the application actually refer to TNF-R(I) using its alternative name – TNF-R p55. Both of these names are widely used and it is commonly understood in the art that they refer to the same TNF-R superfamily member. For example, the Greene PCT[1] discusses the receptors for the ligand TNF-α and TNF-β and teaches that:

> [b]oth molecules [TNF-α and TNF-β] are active as homotrimers and mediate similar biologtical effects by binding to the same two cellular receptors of 55 kD (p55 or complex I) and 75kD (p75) molecular weight.[2]

The Greene PCT subsequently refers to these receptors as TNF-R p55 and p75, respectively.[3] Thus, it is clear that the 55 kD TNF receptor is known alternately as TNF-R p55 and TNF-R(I) (*i.e.*, TNF-R complex I).

A review of the instant specification reveals that this application also refers to the receptors using both of its art recognized names -- TNF-R p55 and TNF-R(I). For

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[1] International Patent Publication No. WO 98/53842. This reference was cited by the Examiner in the previous Office Action so that the reference is already of record in this application.

[2] See, in particular, the Greene PCT at page 1, lines 32-35 (citing Smith *et al.*, *Science* 1990, 248:1019; and Schall *et al.*, *Cell* 1990, 61:361).

[3] See, for example, in the Greene PCT (WO/98/53842) at page 2, line 1.

example, the Examiner's attention is particularly directed to lines 1-5 on page 37 of the application as filed. This paragraph describes cDNA constructs used to express chimeric proteins of the TNF receptor, and notes that the construct expresses the extracellular domain of "TNF-R(I) or p55." The paragraph then cites two references that describe the constructs used in that example[4], and these reference clearly explain that the construct encodes a fusion protein of the 55 kD TNF receptor.

In summary, it is clear from both this application as filed and the art already of record that the 55 kD receptor for TNF ligand is commonly known by two established names: TNF-R(I) and TNF-R p55. Although both of these names may be used in the application, it is clear that they refer to the same TNF receptor. Hence, the limitation of TNF-R(I) is fully supported in the application as filed.

Respectfully submitted,

Dated: June 4, 2003

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[4] In particular, citations are made to the references Peppel *et al., J. Exp. Med.* 1991, 174:1483; and Williams *et al., Immunol.* 1995, 84:433. These references are cited as references BS and CF, respectively, in the Information Disclosure Statement mailed March 28, 2001 for this application. The references therefore are already of record in this application, and its believed that the Examiner already has copies of these references. Nevertheless, Applicants will be happy to provide additional courtesy copies to the Examiner upon request.